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B. Webb
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Patent
Attorney's Docket No. 028723-020

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Joe Gray et al.	)	Group Art Unit: 1634
	)	
Application No. 08/487,701	)	Examiner: A. Marschel
	)	
Filed: June 7, 1995	)	Appeal No.
	)	
For: METHODS FOR STAINING TARGET CHROMOSOMAL DNA EMPLOYING HIGH COMPLEXITY NUCLEIC ACID PROBES	)	

BRIEF FOR APPELLANT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This appeal is from the decision of the Primary Examiner dated May 29, 1998 (Paper No. 44), finally rejecting claims 48-69, which are reproduced as an Appendix to this brief.

Authority to charge the [] $150.00 [X] $300.00 requisite Government fee to Deposit Account No. 02-4800 and two extra copies of this brief are being filed herewith.

The Commissioner is authorized to charge any fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

I. Real Party in Interest

The present application is assigned of record to The Regents of the University of California.

II. Related Appeals and Interferences

No other appeals or interferences that will directly affect or be directly affected by the Board's decision in the instant appeal are known either to Applicants, to their Assignees, or to Applicants' undersigned representative.

II. Status of Claims

The status of the claims as set out in Paper No. 46 was and is as follows:

Allowed Claims: 72-86, 88-93 and 95-97

Claims Objected To: 71

Claims Rejected: 48-69

III. Status of Amendments

The Amendment dated August 31, 1998 was deemed not to place the application in condition for allowance. However, the Examiner indicated that upon filing of a appeal, the Amendment dated August 31, 1998, would be entered.

IV. Summary of the Invention

Applicants' invention is directed to a method of staining target chromosomal material using nucleic acid probes which are substantially complementary to unique nucleic acid segments.

V. The Issue

The Examiner has rejected claims 48-69 as purportedly being obvious over claims 1-17 of U.S. Patent No. 5,447,841 (hereinafter '841).

VI. Grouping of Claims

For the purposes of the rejection of claims 48-69 under the judicially created doctrine of obviousness-type double patenting, it is Applicants's intention that those claims stand or fall together.

VII. Argument

The Examiner has rejected claims 48-69 as purportedly being obvious over claims 1-17 of U.S. Patent No. 5,447,841 (hereinafter '841). Claim 1 of the '841 Patent, and the claims that depend therefrom, is distinguishable from claim 48 of the instant application, and the claims that depend therefrom, because the claims in the instant application require probes which are (1) greater than 40 kb which are targeted to (2) unique nucleic acid segments in the chromosome. Claim 1 of the '841 patent does not recite these two functional limitations. Accordingly, claims 48-69 of the present application are not *prima facie* obvious over claim 1 of the '841 Patent.

VIII. Conclusion

For the foregoing reasons, it is submitted that the Examiner's rejection of claims 48-69 was erroneous and reversal of his decision is respectfully requested.

Respectfully submitted,

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APPENDIX

The Appealed Claims

48. A method of staining target chromosomal material comprising:

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb, which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal material for which detection is desired, and providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid; and

(b) employing said labeled nucleic acid probe, blocking nucleic acid, and chromosomal DNA in in situ hybridization so that labeled repetitive segments, if present, are substantially blocked from binding to the chromosomal DNA, while hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, wherein blocking of the labeled repetitive segments is sufficient to permit detection of hybridized labeled nucleic acid containing unique segments, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the in situ hybridization.

49. The method of claim 48, wherein the chromosomal DNA is present in a morphologically identifiable chromosome.

50. The method of claim 48, wherein the chromosomal DNA is present in a cell nucleus during the in situ hybridization.

51. The method of claim 48, wherein the chromosomal material is from a fetal cell.

52. The method of claim 49, further comprising the step of separating the fetal cell from maternal blood.

53. The method of claim 48, wherein the labeled nucleic acid probe comprises heterogeneous mixtures of labeled nucleic acid fragments, wherein the nucleic acid fragments are substantially complementary to sites on the targeted chromosomal material and are substantially free of nucleic acid sequences having a hybridization capacity to sites on chromosomal material that is not targeted.

54. The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing chromosomes.

55. The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing portions of a chromosome.

56. The method of claim 48, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of chromosomal rearrangement.

57. The method of claim 56, wherein the chromosomal rearrangement is an inversion.

58. The method of claim 56, wherein the chromosomal rearrangement is an insertion.

59. The method of claim 56, wherein the chromosomal rearrangement is a translocation.

60. The method of claim 56, wherein the chromosomal rearrangement is an amplification.

61. The method of claim 56, wherein the chromosomal rearrangement is a deletion.

62. The method of claim 48, wherein the target chromosomal material is present in an interphase cell nucleus.

63. The method of claim 62, wherein the labeled nucleic acid has a complexity of between about 40 kb and 100 kb.

64. The method of claim 62, wherein the labeled nucleic acid has a complexity between about 50 kb and 400 kb.

65. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to the total genomic complement of chromosomes.

66. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a single chromosome.

67. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a subset of chromosomes.

68. The method of claim 48, wherein the labeled nucleic acid comprises fragments complementary to a subregion of a single chromosome.

69. The method of claim 48, wherein the labeled nucleic acid is designed to allow detection of cancer.

71. The method of claim 48, further comprising removing from the labeled nucleic acid fragments which are substantially complementary to repetitive segments within the target chromosomal material.

72. A method of staining target interphase chromosomal DNA comprising:

(a) providing at least one labeled nucleic acid probe having a complexity greater than about 40 kb which labeled nucleic acid probe comprises fragments which are substantially complementary to unique nucleic acid segments within the chromosomal DNA for which detection is desired, wherein the nucleic acid probe is substantially free of repetitive segments which are complementary to repetitive segments in the target interphase chromosomal material; and

(b) employing said labeled nucleic acid probe and chromosomal DNA in in situ hybridization so that hybridization of unique segments within the labeled nucleic acid probe to the chromosomal DNA is allowed, and hybridized labeled nucleic acid containing unique segments are detected, and wherein the interphase chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the in situ hybridization.

73. The method of claim 72, further comprising providing blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid probe and employing said blocking nucleic acid in in situ hybridization so that labeled repetitive segments, if present, are substantially blocked from binding to the chromosomal DNA.

74. The method of claim 72, wherein the chromosomal DNA is present in a morphologically identifiable chromosome.

75. The method of claim 72, wherein the chromosomal DNA is present in a cell nucleus during the in situ hybridization.

76. The method of claim 72, wherein the chromosomal material is from a fetal cell.

77. The method of claim 76, further comprising the step of separating the fetal cell from maternal blood.

78. The method of claim 72, wherein the labeled nucleic acid probe comprises heterogeneous mixtures of labeled nucleic acid fragments, wherein the nucleic acid fragments are substantially complementary to sites on the targeted chromosomal material and are substantially free of nucleic acid sequences having a hybridization capacity to sites on chromosomal material that is not targeted.

79. The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing chromosomes.

80. The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of extra or missing portions of a chromosome.

81. The method of claim 72, wherein the labeled nucleic acid probe comprises fragments which are designed to allow detection of chromosomal rearrangement.

82. The method of claim 81, wherein the chromosomal rearrangement is an inversion.

83. The method of claim 81, wherein the chromosomal rearrangement is an insertion.

84. The method of claim 81, wherein the chromosomal rearrangement is a translocation.

85. The method of claim 81, wherein the chromosomal rearrangement is an amplification.

86. The method of claim 81, wherein the chromosomal rearrangement is a deletion.

88. The method of claim 87, wherein the labeled nucleic acid has a complexity of between about 40 kb and 100 kb.

89. The method of claim 87, wherein the labeled nucleic acid has a complexity between about 50 kb and 100 kb.

90. The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to the total genomic complement of chromosomes.

91. The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to a single chromosome.

92. The method of claim 72, wherein the labeled nucleic acid comprises fragments complementary to a subregion of a single chromosome.

93. The method of claim 72, wherein the labeled nucleic acid is designed to allow detection of cancer.

95. The method of claim 72, wherein the targeted chromosomal material is a genetic rearrangement associated with chromosome 21 in humans.

96. The method of claim 72, wherein fragments substantially complementary to repetitive segments in the target interphase chromosomal material have been removed from the labeled nucleic acid probe.

97. The method of claim 72, wherein the complexity of the labeled nucleic acid probe is greater than about 200 kb.